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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,495	01/02/2002	Wen Liang Yan	0249-0002US	7029

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,495	YAN ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HL

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 2, 2005 has been entered.

The amendment, declaration, and response filed on 12/20/04, 1/24/05, and 3/2/05 have been entered. Claims 29 and 31 have been amended. Claims 1-28 and 30 have been canceled. Claims 29 and 31-33 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the declaration, response, and amendment to pending claims will not be reiterated. The arguments in 12/20/05 and 3/2/05 responses would be addressed to the extent that they apply to current rejection.

Specification

The amendments to the specification do not comply with the Revised Amendment Practice of 37 CFR 1.121 (See the MPEP § 714 II-B), which requires that amendments to the specification, other than the claims, computer listings (37 CFR1.96) and sequence listings (37 CFR 1.825), must be made by adding, deleting or replacing a

paragraph, by replacing a section, or by a substitute specification. In order to delete, replace or add a paragraph to the specification of an application, the amendment must unambiguously identify the paragraph to be modified either by paragraph number (see MPEP § 608.01), page and line, or any other unambiguous method and be accompanied by any replacement or new paragraph(s). The 12/20/04 amendment contains pages of text insertion to the originally filed specification without replacing the entire paragraph or section. Thus the amendment fails to comply with the requirement set forth in MPEP.

A full response to this Office Action must include a complete response that complies with the formality requirement of the amendment.

Claim Rejections

Claim 29 is objected to because the acronym "HS" should be defined the first time it appears in the claim, the amendment defines "HS" only when the second time it appears in the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 31-33 stand and newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is vague and indefinite because the claim recitation "immunotyped". The term "immunotype" encompasses many different features associated with an immune response such as MHC haplotype, antibody serotypes, and the types of complement system. The amended claims limit the HS cells to "homozygous for the MHC haplotypes" in the preamble, but not the method steps. The claims should be amended to reflect this limitation whenever "immunotype" appears.

Claim 29 is vague and indefinite because it is unclear which noun the phrase "from multiple donors" defines, haplotypes, or stem cells, and thus the metes and bounds of the claims are unclear.

Claim 29 is vague and indefinite because according to the teaching of the specification, the claimed HS cell depository contains various stem cell lines from multiple donors, each donor may have a MHC haplotype that is distinct from others, yet the claim reads on a cell depository wherein all of the HS cells are homozygous for a MHC haplotype. Thus the metes and bounds of the claims are uncertain.

Claim 29 is vague and indefinite because of the claim recitation, "HS cells that are homozygous for the Major Histocompatibility Complex haplotypes". Homozygous is a term reserved for describing genomic make-up of an allele, not suitable for describing the cells.

Claim 29 recites "the Major Histocompatibility Complex haplotypes". There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29 and 31-33 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a *mouse* HS cell line via mitotically activating non-fertilized female post-meiosis I diploid germ cells with *ionomycin and DMAP*, does not reasonably provide enablement for making a human HS cell line or making a non-human mammalian HS cell line via any type of mitotic activation, and it does not reasonably provide enablement for using the mammalian embryonic stem (ES) cell lines for therapeutic transplantation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

The claims are drawn to a method for producing a pluripotent embryonic stem cell depository, wherein the genome of each line of stem cells in the depository is homozygous for its MHC haplotype, i.e. a particular combination of MHC alleles found on an individual chromosome is the same as found on the other chromosome, wherein the stem cells of the depository are produced by mitotically activating post-meiosis I diploid and non-fertilized oocyte. The specification teaches that these cells are desirable for preventing immune rejection when used for transplantation.

Given the broadest reasonable interpretation, the claimed method encompasses any means of mitotic activation. The specification refers to conventional methods known in the art for mitotic activation of parthenogenetic oocytes. In working examples, the specification teaches combined ionomycin and DMAP for parthenogenetic oocyte activation. In view of the state of the art, numerous means have been used for parthenogenetic activation of oocytes. For example, *Mitalipov et al* (Biol Reproduct 2001;65:253-9) compared several activation means for *in vitro* development of monkey parthenotes (table II), and teach ionomycin alone fails to activate rhesus monkey oocytes, but when ionomycin and DMAP were combined, the oocytes underwent mitotic division. *Newman-Smith et al* (Development 1995;121:2069-77) use ethanol and cytochlasin D for parthenogenetic mouse oocyte activation, the stem cells isolated from the parthenogenetic ICM have both a proliferation defect and a cell fate defect, and thus not suitable for developing HS cell lines. Apparently, many factors may influence the mitotic capability of parthenotes from which pluripotent stem cells could be obtained, and these factors have yet to be clearly defined. Thus, the disclosure of the

specification concerning the conditions for activating non-fertilized oocytes in order to obtain mouse embryonic stem cell lines is insufficient to support the broad claims that encompass any means of activation. Since the specification fails to teach other means of mitotically activating non-fertilized post-meiosis I diploid female germ cells that would lead to establishment of ES cell lines with homozygous MHC haplotypes, and in view of the contradictory evidence found in the references, the claimed invention does appear to be enabled for the full scope in the absence of clarification to the contrary.

Claim 32 clearly indicates the invention is drawn to creating a human ES cell depository for transplantation. To this end, the therapeutic potential of establishing an embryonic stem cell bank and the vision of obtaining homozygous stem cells from parthenogenetic ES cells are known in the art. For example, *Gearhart* (Science 1998;282:1061-2) teaches, "IN ADDITION TO POSSIBLY PROVIDING LARGE NUMBERS OF PURE POPULATIONS OF CELLS FOR TRANSPLANTATION, ES CELLS WOULD ALSO LEND THEMSELVES TO SEVERAL STRATEGIES FOR THE PREVENTION OF IMMUNOLOGICALL TISSUE REJECTION AFTER TRANSPLANTATION, INCLUDING (I) **BANKING OF MULTIPLE ES CELL LINES REPRESENTING A SPECTRUM OF MAJOR HISTOCOMPATIBILITY COMPLEX** (MHC) ALLELES TO SERVE AS A SOURCE FOR HC MATCHING..." (column 3, page 1061). *Liu et al* teach "THE ESTABLISHMENT OF PARTHENOGENETIC ES CELL LINE ...DEMONSTRATES THAT IT IS POSSIBLE TO DERIVE CELL LINES OF HOMOZYGOUS DIPLOID GENETIC CONSTITUTION FROM HAPLOID EMBRYOS" (1st paragraph, page 247). However, establishing human ES lines from parthenogenetic ES cells has not become practical in the art at the time of instant priority date, and has not become routine after the filing date of instant application. For example, as indicated previously, the applicants acknowledge they fail to obtain human HS cell lines as of a post-filing

date (Lin et al, Stem Cells 2003;21:152-61). Applicants admitted "SO FAR, FURTHER CULTURING OF THE [human] INNER CELL MASSES PRODUCED BY THIS ACTIVATION METHOD HAS NOT BEEN SUCCESSFUL" (mid-section, right column, page 158). In the declaration submitted 12/20/04, Dr. Huang cited four post-filing art from different study groups as support for enablement of instantly claimed invention. Of the four references, *Hwang et al* specifically teach obtaining a pluripotent *human* embryonic stem cell line. However, it is noted the starting materials and protocols used by *Hwang et al* differ from instantly claimed and disclosed. *Hwang et al* use an oocyte manipulated by somatic cell nuclear transfer (SCNT) as the starting material, the mitotic activation was performed after the SCNT, at a non-specified stage, (at the least not homogeneously post-meiosis I diploid female germ cells). The activating chemical was A23187, not ionomycin; and the ES cell culture protocol also differs from instantly disclosed. These subtle differences may well be or at least partially responsible for the success of *Hwang et al* in the absence of evidence to the contrary. Thus, the Hwang reference does not appear to fully support the claimed invention.

Another barrier for successfully establishing ES cell lines from parthenogenetic ICMs lies on cultivation technology. To this end, the art is still under development, many conditions are yet to be delineated. For example, *Gearhart* (Science 1998;282:1061-2) teaches, "TO REALIZE THE FULL POTENTIAL OF HUMAN PLURIPOTENT STEM CELLS, CHALLENGING RESEARCH LIES AHEAD AND SERVAL PRACTICAL ISSUES MUST BE RESOLVED. THE CONDITIONS NECESSARY TO DERIVE HUMAN ES CELLS EFFICIENTLY AND RELIABLY MUST BE DEFINED. HOW DID THE THOMSON GROUP SUCCEED WHEN, ON THE SURFACE THEIR PROTOCOL IS SO SIMILAR TO THAT OF OTHER INVESTIGATORS?" (paragraph bridging 1061-2). In addition to the oocyte

activation step (as taught by *Mitalipov et al*), *Newman-Smith* et al have shown many genes in the embryonic development stage are critical for whether the stem cell population could be maintained and propagated. They concluded that parthenogenetic ICM cells have both a proliferation defect and a cell fate defect owing to miscegenation of genes critical to growth and differentiation. *Taylor et al* (1994, IDS) teach that although the timing of developmental events is similar to that seen in fertilized oocytes, the developmental potential of human parthenogenetic embryos was reduced, and the majority of those allowed to continue in co-culture arrested between the 2-cell, and 8-cell stages (abstract). In 12/20/04 response, applicants argue that although the *Taylor* reference showed a reduced rate and eventual cell arrest, it still shows the ability to parthenogenetically activate human oocytes. In reply, it is noted the claimed invention is drawn to producing an ES cell depository, therefore, unless the ES cell lines be established, the claimed invention is not fully enabled.

Moreover, the intended use of the ES cell bank is drawn to providing human ES cells for therapeutic transplantation using the ES cell depository to prevent host immune rejection. However, neither prior art of record nor the specification provides adequate disclosure to show such cells could indeed be used in human stem cell therapy. In fact, numerous art of record pointed to the contrary. In a post-filing publication, *Draper et al* (Curr Opin Obstet Gynecol 2002;14:309-315) teach, "CURRENT RESULTS DO INDICATE THAT DIFFERETIATION OF HUMAN PLURIPOTENT STEM CELLS INTO A RANGE OF CLINICALLY USEFUL CELL TYPES IS POSSIBLE. HOWEVER, CONSIDERABLE RESEARCH IS NECESSARY BEFORE TREATMENTS USING TRANSPLANTATION OF HPSC-DERIVED TISSUES MAY BECOME A PRACTICAL REALITY" (right

column, page 309, emphasis added). *Donovan and Gearhart* (Nat 2001 Nov;414:92-97) teach "IF STEM CELLS ARE TO BE USED TO TREAT A WIDE VARIETY OF HUMAN DISEASES, THEN WE WILL NEED TO OVERCOME SEVERAL FORMIDABLE CHALLENGES. STEM CELLS WILL BE NEEDED IN LARGE QUANTITIES AND BE ABLE TO DIFFERENTIATED IN A CONTROLLED MANNER TO FORM HOMOGENEOUS POPULATIONS OF CELLS THAT ARE HISTOCOMPATIBLE WITH AN INDIVIDUAL" (left column on page 95). *Odorico et al* (Stem Cells 2001;19:193-204) detailed the major barriers for using EM stem cell lines for routine therapeutic purpose. They teach that the efforts have been hampered a). by the inability to selectively differentiating human ES cells to a particular cell type of interest and to purify this lineage from the mixed population; b). by the inability to demonstrate that the differentiated cells and cellular derivatives function in a normal physiologic way, because differentiated ES cell cultures can contain multipotent progenitors as well as terminally differentiated cells. Many fetal or embryonic tissues and multipotent cells are functionally immature, one cannot assume that all ES cell progeny will subserve normal cellular physiologic functions; c). by the requirement of integration of the transplanted cells into the existing host tissue in a functionally useful form; d). by the possibility that human ES cell derivatives may form tumors in human recipients (see particularly, pages 198-200). The specification fails to teach how to overcome the aforementioned difficulties in the art. It would have required undue experimentation for the skilled artisan intending to practice the instant invention. In the response and declaration, applicants fail to address this important issue, accordingly, it is maintained that the disclosure fails to enable the intended use for producing an ES cell depository.

In the Remarks filed 3/2/05, applicants discussed parthenogenetic teratoma as supporting evidence. However, a teratoma comprises many different cell types, which are uncontrollably differentiated and at various developmental stages, and thus could not be used for therapeutic purpose. This is one of the barriers yet to be conquered if human ES cells are to be used for therapeutic purpose.

While, the intent for citing the references is not to say that human homozygous ES cell line can never be readily obtained and used for therapy in a future time, the intent is to provide art taught reasoning as to why the instant claims are not enabled at the time of instant priority date, and to illustrate the general state of the art in establishing human ES cell lines from parthenogenetic embryos, and using such for therapeutic purpose. Since the skilled artisans have only limited knowledge concerning what it takes to successfully establish pluripotent ES cell lines, and concerning the underlying mechanism that leads to the success of *Hwang et al.* The fact that instant applicants have yet to obtain human HS cell line even at a post-filing date indicates the unpredictability of the art, and underdeveloped state of the art. Since the claimed human HS cells cannot be readily and reproducibly generated at the time of the instant filing, it would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Accordingly, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 31, 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Gearhart* (Science 1998;282:1061-2), in view of *Liu et al* (Acta Zoologica Sinica 1998;44:247-8), *Stice et al* (US 6,235,970), and *Ohnuma et al* (J Hematother Stem Cell Res 2000;9:541-550).

Gearhart (Science 1998;282:1061-2) teaches the need for establishing an embryonic stem cell bank for providing stem cells with diverse MHC haplotypes, "IN ADDITION TO POSSIBLY PROVIDING LARGE NUMBERS OF PURE POPULATIONS OF CELLS FOR TRANSPLANTATION, ES CELLS WOULD ALSO LEND THEMSELVES TO SEVERAL STRATEGIES FOR THE PREVENTION OF IMMUNOLOGICALL TISSUE REJECTION AFTER TRANSPLANTATION, INCLUDING (I) **BANKING OF MULTIPLE ES CELL LINES REPRESENTING A SPECTRUM OF MAJOR HISTOCOMPATIBILITY COMPLEX** (MHC) ALLELES TO SERVE AS A SOURCE FOR HC MATCHING..." (column 3, page 1061). *Gearhart* does not teach deriving such ES cell lines from parthenogenetic ICMs.

Liu et al supplemented the teaching of *Gearhart* by establishing the levels of the skilled in the art concerning obtaining stem cells from parthenogenetic blastocysts. *Liu et al* teach that they generated ES cell lines from ICM of delayed parthenogenetic mouse embryos (table I) in order to obtain ES cells with homozygous diploid genetic constitution "THE ESTABLISHMENT OF PARTHENOGENETIC ES CELL LINE ...DEMONSTRATES THAT IT IS POSSIBLE TO DERIVE CELL LINES OF HOMOZYGOUS DIPLOID GENETIC CONSTITUTION FROM HAPLOID EMBRYOS" (e.g. 1st paragraph, page 247). Although *Liu et al* do not particularly teach the homozygosis should be at MHC alleles, *Gearhart* and *Ohnuma et al* have suggested so.

Stice et al supplemented the teaching of *Gearhart* by establishing the levels of the skilled in the art concerning obtaining bovine and porcine stem cells from parthenogenetic blastocysts. They teach a method for obtaining bovine and porcine ES cell lines from parthenogenetically activated ICMs (e.g. claim 1 and col 17, lines 13-39).

Ohnuma et al supplemented the teachings of *Gearhart* and *Liu et al* by establishing the levels of the skilled on MHC genotyping and importance of MHC compatibility on clinical outcome of stem cell transplantation. *Ohnuma et al* teach the techniques of typing HLA (human MHC), and found that incompatibility of two or more HLA-alleles between the donor and recipient is a risk factor for a worse event-free survival in allogeneic cord blood transplantation.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to establish a mammalian ES cell depository as suggested by *Gearhart et al,* using the techniques as taught by *Liu, Stice et al,* and *Ohnuma et al* with a reasonable expectation of success. The ordinary skilled artisan would have been

motivated to do so because the ES cells homozygous for MHC haplotype would reduce the risk of allogenic stem cell transplantation. Given the success of *Liu et al, Stice et al* in establishing parthenogenetically-derived mouse, porcine, and bovine stem cell lines, one would have had a reasonable expectation of success in establishing a parthenogenetic mammalian ES cell depository, wherein the genome of each line of the ES cells is homozygous for MHC haplotype. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Request for Interview

The examiner acknowledges applicant's request for an interview, and called Mr. Herbert's Office on April 7, 2005 to discuss the possibility of conducting an interview even though the requested date had passed when the examiner noticed the request. A message was left with the secretary, and no response had been received at the time this Office action was issued.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
April 18, 2005